**Remarks**

The non-final Office Action dated June 9, 2006 has been reviewed and the following remarks are made in response thereto. Upon entry of the instant amendment, Claims 15, 17, 25, 27, 32 and 40 are pending. Claims 32 and 40 are amended. Written support for the claim amendments are found throughout the specification and in the original claims, thus Applicants submit that no prohibited new matter has been added. In view of the above amendments and following remarks, Applicants respectfully request reconsideration of this application and timely allowance of the pending claims

Rejections under 35 U.S.C. 112 (second paragraph)

Claim 32 was rejected under 35 U.S.C. 112 (second paragraph) as being indefinite. Specifically, the Examiner alleged that the recitation "the nucleic acid" in claim 32 lacks proper antecedent basis because claims 15 and 17 from which it depends do not recite a nucleic acid.

Without acquiescing to the merits of the Examiner's rejection, and solely to expedite prosecution of the instant application, Applicants have amended claim 32 to recite that the chondrocyte comprises "one of the DNAs of claims 15 and 17, or one of the nucleic acids of claims 25 and 27." As such, amended claim 32 has proper antecedent basis in claims 15, 17, 25 and 27. Accordingly, Applicants request that the rejection of claim 32 under 35 U.S.C. 112 (second paragraph) be withdrawn.

Rejections under 35 U.S.C. 101

Claims 15, 17, 25, 27, 32 and 40 were rejected under 35 U.S.C 101 because the claimed invention was allegedly neither supported by a specific asserted utility nor a well established utility. Applicants respectfully traverse the rejection.

It is unclear to Applicants why claims 15, 17, 25, 27 were rejected for lack of utility under 35 U.S.C 101. These claims were allowed on November 8, 2005 as evidenced by the Notice of Allowance issued by this Examiner. Applicants are unaware of any change in the standards for utility under 35 U.S.C. 101 since November 8, 2005. It is therefore unclear to Applicants why these same claims now purportedly lack utility in the opinion of the Examiner. Applicants submit that the rejection is improper and request that it be withdrawn.

Without acquiescing to the merits of the rejection, Applicants respectfully submit that the specification provides a detailed discussion as to why CDEP is predicted to be a member of the Rho-GEF family, thereby suggesting that CDEP plays an important role in controlling the adhesion, diffusion, migration, proliferation, and differentiation of cells, including chondrocytes (specification, page 12, lines 1-19; see also pages 33-35). As such, the instantly claimed nucleic acids may be used at the very least to

distinguish differentiated cells from non-differentiated or dedifferentiated cells, and particularly differentiated chondrocytes. Such utility is further supported by the fact that CDEP was identified using subtractive hybridization to identify RNAs expressed in differentiated chondrocytes but not dedifferentiated chondrocytes (specification page 2, lines 1-5, and page 26, lines 1-19). Further support is provided by experiments which demonstrated that expression of CDEP is elevated in the presence of parathyroid hormone (PTH) and cAMP, which are known to modulate the differentiation of chondrocytes (specification page 32, lines 6-8).

Furthermore, as a gene involved in chondrocyte differentiation, CDEP may be used to induce or maintain the differentiation of chondrocytes (specification page 34, lines 23-24). Such a use makes it possible to control the differentiated state of chondrocytes playing roles in arthropathies such as osteoarthritis (specification, pages 34-35). In addition, since other Rho-GEF family members are known to become oncogenes as a result of certain N-terminal deletions, CDEP serves as a target for the design of new cancer therapeutics if it shows the same oncogenic potential as other Rho-GEF family members (specification, page 35, lines 3-10). Importantly, the Examiner acknowledges that the additional asserted utilities such as therapy of osteoarthritis and rheumatoid arthritis, and screening regulators of cell differentiation, are predicted utilities based on homologies to ezrin, Dbl and pleckstrin. However, the Examiner questions whether CDEP would have the same functions as these homologous proteins because homology is not 100%, and sequence dissimilarities upon protein structure and function allegedly cannot be predicted.

Applicants respectfully submit that it is perfectly acceptable to predict a specific utility based on membership in a well-known family of conserved proteins, as the comments accompanying the Utility Guidelines specifically state. For instance, according to the comments and answers published in the Federal Register with the new utility examination guidelines (FR, Vol. 66, No. 4, January 5, 2001), it is perfectly acceptable to assert a specific, substantial and credible utility on the basis of "homology to existing nucleic acids or proteins having an accepted utility." Furthermore, according to this notice, a rigorous correlation is not necessary, only a "reasonable" correlation (see the FR notice, page 1096, middle column continuing into the right hand column). As stated therein, "When a class of proteins is defined such that the members share a specific, substantial, and credible utility, the reasonable assignment of a new protein to the class of sufficiently conserved proteins would impute the same specific, substantial, and credible utility to the assigned protein." In fact, according to the new utility guidelines, "the asserted utility *must* be accepted by the examiner unless the Office has sufficient or sound reasoning to rebut such an assertion."

The Examiner purported that single amino acid substitutions can affect the function of a protein.

Applicants note that many proteins with highly divergent sequences have the same activity (e.g. kinases). Those of skill in the art recognize that sequence homologies make it possible to predict protein structure and function. For instance, according to an article by Lisa Holm (Current Opinion in Struct. Biol. (1998) 8:372-79, previously submitted), homology is "a most useful concept in computational biology. By inferring homology between two proteins on the basis of sequence similarity, biologists can confidently predict that protein structure and function have also remained similar in evolution" (page 372, col. 1). According to Holm, a "widely used empirical calibration suggested a threshold of 25-30% sequence identity, above which sequence similarity implies structural (and functional) similarity" (page 372, col. 2).

Notably, Applicants have not predicted the Rho-GEF activity of CDEP based on sequence data alone, but also in view of the experimental data reported in the specification, *i.e.*, that CDEP expression is associated with cellular differentiation and changes in morphology, as might be expected for a Rho-GEF protein serving as a regulatory factor for cytoskeleton binding (specification, page 34, lines 5-21). Importantly, the homologies identified in the specification are within the acceptable range of utility for making predictions regarding protein function (specification, page 10).

Finally, according to the Examiner's reasoning, even if CDEP expression was specific for differentiated chondrocytes, this still would not satisfy the new utility standards because other nucleic acids are specific for differentiated chondrocytes. Therefore, the asserted utility would still not be "specific" to CDEP.

Applicants respectfully submit that, CDEP need not be specific for differentiated chondrocytes for it to have utility in identifying the same. Applicants have shown that CDEP is expressed in differentiated chondrocytes but not in dedifferentiated chondrocytes, which is the only distinction that need be shown for probes designed from CDEP to have utility in chondrocyte-specific differentiation assays. The fact that it is expressed in other cells may mean that it will find a similar utility in the study of other tissues.

In view of all the remarks submitted above, applicants respectfully request that the rejection of claims 15, 17, 25, 27, 32 and 40 under 35 U.S.C. 101 be reconsidered and withdrawn.

Rejections under 35 U.S.C. 112 (first paragraph)

Claims 15, 17, 25, 27, 32 and 40 were rejected under 35 U.S.C. 112 (first paragraph) as failing to comply with the enablement requirement. In particular, the Examiner alleged that the skilled artisan would not know how to use the claimed invention since it lacked utility. Applicants respectfully traverse the rejection.

In view of the arguments presented immediately above, Applicants submit that the instant claims have utility and thus are enabled. Accordingly, Applicants request that the rejection of claims 15, 17, 25, 27, 32 and 40 under 35 U.S.C. 112 (first paragraph) be reconsidered and withdrawn.

Furthermore, claim 40 was rejected under 35 U.S.C. 112 (first paragraph) as failing to comply with the written description requirement. Specifically, the Examiner alleged that claim 40 encompasses a genus of CDEP variants of SEQ ID NO: 1 having at least 80% similarity with SEQ ID NO: 1, with unknown structure and function. Applicants respectfully traverse the rejection.

The P.T.O.'s own revised interim guidelines concerning compliance with the written description requirement, provide that the disclosure of identifying characteristics such as partial structure, functional characteristics and method of making must all be weighed in view of the level of skill and the knowledge in the art and in the light and consistent with the written description (66 Fed. Reg. 1099 (2001)). Rather than require a recitation of each and every DNA and peptide sequence sought to be claimed by a patentee, courts have recognized that the descriptive text needed to meet the requirements of written description varies with the nature and scope of the invention at issue, and with the scientific and technologic knowledge already in existence (*Capon v. Eshhar*, 76 U.S.P.Q.2d 1078, 1084 (Fed. Cir. 2005)).

Applicants submit that, in contrast to what is alleged in the Office Action, the instant specification sets forth common structural attributes of the claimed nucleic acids and the specification provides guidance as to which portions of the nucleic acids may contain substitutions. Additionally, the specification specifically indicates which substitutions would be most tolerated (specification, page 14, lines 12-18). Given that the level of skill in the art of modifying nucleic acids was high at the time the instant application was filed, the skilled artisan would be capable of using the disclosure in the specification to arrive at the instantly claimed genus of variant nucleotides. Accordingly, Applicants request that the rejection of claim 40 under 35 U.S.C. 112(first paragraph) be reconsidered and withdrawn.

Rejections under 35 U.S.C. 102

Claim 40 was rejected under 35 U.S.C. 102(e) as being anticipated by Studier (U.S. Patent 5,407,799) ("Studier"). In particular, the Examiner alleged that the oligonucleotides taught by Studier would hybridize to the nucleotide sequence ranging from the 49th to the 3,183rd bases of SEQ ID NO: 1 under the hybridization conditions cited in claim 40.

Without acquiescing to the merits of the Examiner's rejection, and solely to expedite prosecution of the instant application, Applicants have amended claim 40 to specify that the claimed DNA molecule hybridizes under stringent conditions to nucleotides from position 49 through position 3,183 of SEQ ID

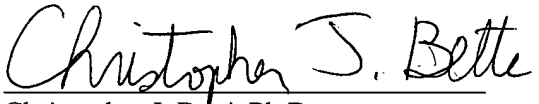
NO: 1. Given that the oligonucleotides of Studier do not hybridize over the entire length of nucleotides 49th to 3,183rd bases of SEQ ID NO: 1, Applicants request that the rejection of claim 40 under 35 U.S.C. 102(e) be reconsidered and withdrawn.

Conclusion

The foregoing amendments and remarks are being made to place the application in condition for allowance. Applicants respectfully request entry of the amendments, reconsideration, and the timely allowance of the pending claims. A favorable action is awaited. Should the Examiner find that an interview would be helpful to further prosecution of this application, they are invited to telephone the undersigned at their convenience.

If there are any additional fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-0310. If a fee is required for an extension of time under 37 C.F.R. 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted
**Morgan, Lewis & Bockius LLP**



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Dated: **December 8, 2006**
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